DETAILED ACTION

Withdrawn Rejections

The rejection of claims 1, 2, 4-6, 8-30 and 38-40 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn after further consideration of the rejection.

The rejection of claim 7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been withdrawn in view of applicants amendments to the claim.

The rejection of claims 13 and 17 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps has been withdrawn in view of applicant's cancellation of claims 13 and 17.

The rejection of claim 14 under 35 U.S.C. 102(b) as being anticipated by Allen et al. (Hepatology, 1998;27:1670-1677) has been withdrawn in view of applicant's cancellation of claim 14.

The rejection of claims 22 and 26 under 35 U.S.C. 102(b) as being anticipated by Zaaijer et al. (J Clin Microbiol, 1994, 32(9):2088-2091) has been withdrawn in view of applicant's amendment to the claims. Zaaijer et al. does not teach a means for obtaining the nucleic acid sequence of the HBV.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-6, 8-12, 15, 16, 18-30 and 38-40 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Because there is no reference sequence provided and because the open language "comprising" is used to describe the HBV polynucleic acid length, one of ordinary skill in the art would not know where position 204 is located. The claims encompass a large genus of polynucleotides of varying sizes, and counting from the first codon of these sequences will give a different result for position 204 (or 180). Accordingly, one of ordinary skill in the art cannot determine the metes and bounds of the claims.

Response to Arguments

In the reply dated August 18, 2010 applicant argues that the rejection has been obviated by amendments to the claims. All of applicant's arguments have been fully considered but not found persuasive.

As stated above, the claims encompass a large genus of HBV reverse transcriptase polynucleotides of varying length due to, for example, mutations such as insertions or deletions in the gene/protein. Therefore, one of ordinary skill in the art starting from the first codon of the reverse transcriptase gene will arrive at a different codon for positions 180 and 204. In addition, because of the mutatable nature of DNA,

there is not sufficient guidance to point to a specific position in the reverse transcriptase gene/protein. Without referring to a reference sequence or without "corresponding" language (e.g., comprising a serine encoding codon at the position that corresponds to position 204 of SEQ ID NO: X), one of ordinary skill in the art would not know where serine 204 (or methionine 180) is located in a given sequence.

It is noted that applicant's argued for the 112, first paragraph, rejection that counting of codons in the reverse transcriptase gene is based on the teachings of Stuyver et al. Applicant stated that "consensus numbering of codons has been used throughout the present patent application as filed, as described by Stuyver at all, 2001 (a copy of which was submitted with the Information Disclosure Statement of September 17, 2007). By this consensus numbering of codons this numbering is independent from the HBV genotype as has been exemplified in Table 1, on page 8 of the present patent application. The proposed numbering of the polymerase of HBV's starts with the highly conserved EDWGPCDEHG motif making the total length of the HBV reverse transcriptase/polymerase (rt domain) 344 amino acids long and genotype independent (see page 753, second column of the Stuyver article)."

While the counting method of Stuyver et al. provides sufficient guidance for one of ordinary skill in the art to locate codon 180 or 204 in an HBV reverse transcriptase that is 344 amino acids long, this counting method does not provide sufficient guidance in instances where the HBV reverse transcriptase is, for example, less than 344 due to a deletion. Further, it appears applicant is relying on the method of Stuyver et al. as the sole method for counting amino acids. If this is the case, this is an improper

incorporation by reference of essential material to a publication under 37 CFR 1.57(c). Accordingly, the counting method of Stuyver et al. should be included in the specification because it is essential to practicing the claimed method. Because, applicant has explicitly incorporated by reference recited publications in the specification, applicant can amend the specification to include a full description of the counting method of Stuyver et al. (see 37 CFR 1.57(g)). Otherwise, without such amendment, it will be an improper incorporation by reference.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 18 is rejected under 35 U.S.C. 102(b) as being anticipated by Allen et al. (Hepatology, 1998;27:1670-1677).

The claim is directed to a method for detecting resistance to lamivudine or a combination of antiviral drugs comprising lamivudine of an HBV virus present in a biological sample, said method comprising the step of detecting the presence of an HBV polynucleic acid comprising a reverse transcriptase encoding domain, said reverse transcriptase encoding domain comprising a serine encoding codon at position 204, said method:

(i) obtaining a target HBV polynucleic acid from said biological sample wherein said target HBV polynucleic acid is suspected to comprise a serine-encoding codon at position 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon at position 180 and a serine-encoding codon at position 204 of the HBV reverse transcriptase domain;

(ii) obtaining the nucleic acid sequence of the target HBV polynucleic acid of (i);

(iii) inferring, from the nucleic acid sequence obtained in (ii), the presence of said serine-encoding codon at position 204 in the HBV reverse transcriptase domain or of said methionine-encoding codon at position 180 and said serine-encoding codon at position 204 in the HBV reverse transcriptase domain and, therefrom, said resistance to lamivudine or a combination of antiviral drugs comprising lamivudine of an HBV virus present in said biological sample.

It is noted that the claim is being interpreted as comprising two steps: i) obtaining an HBV polynucleic acid, and (ii) sequences the polynucleic acid. The phrase "suspected to comprise a serine-encoding codon at position 204 . . . ." has no meaning in the claim because it is not known, at the time of performing the method, whether or not the HBV DNA has any mutations at position 204. Further, the inferring step or clause does not recite any additional active method steps, but simply states a characterization or conclusion of the previous step(s) or may be performed entirely in the human mind. Therefore, the "inferring " step or clause is not found to further limit the method defined by the claims, since it simply expresses the intended result of a positively recited process step.

Allen et al. teaches obtaining and sequencing HBV DNA using primers that fall within the HBV polymerase gene. Thus, Allen et al. teaches the claimed method steps, and thus, anticipates claim 18.

Response to Arguments

In the reply dated August 18, 2010, applicant argues that the Examiner's interpretation of claim 18 does not include the requirement to infer from the nucleic acid sequence the presence of the serine encoding codon. Applicant's arguments have been fully considered but not found persuasive.

As stated above, the inferring step or clause does not recite any additional active method steps, but simply states a characterization or conclusion of the previous step(s) or may be performed entirely in the human mind. One observing the claimed method being performed would not know if or when the inferring step has occurred. There is no active method step to observe after step (ii) (obtaining the nucleic acid sequence). Therefore, the "inferring" step or clause is not found to further limit the method defined by the claims, since it simply expresses the intended result of a positively recited process step.

It is suggested that applicant amends part (iii) of claim 18 to recite "analyzing the nucleic acid sequence obtained in (ii) for the presence of . . . ."

Claims 21 and 25 remain rejected under 35 U.S.C. 102(b) as being anticipated by Zaaijer et al. (J Clin Microbiol, 1994, 32(9):2088-2091).

The claims are directed to a diagnostic kit for detecting the presence of an HBV in a biological sample, said kit comprising a means for detecting the presence of an HBV polynucleic acid comprising a reverse transcriptase encoding domain, said reverse transcriptase encoding domain comprising a serine encoding codon at position 204.

It is noted for claims 21 and 25 the claims are interpreted as being directed to a kit for detecting the presence of HBV reverse transcriptase polynucleic acid.

Zaaijer et al. discusses and compares four commercial kits used to detect HBV DNA. The kits use PCR or hybridization to detect HBV DNA from HBsAg and HBeAg (polymerase/reverse transcriptase). These kits, especially the hybridization kits, are sufficient to detect an HBV nucleic acid carrying a single mutation at codon 204 because these kits contain a means for detecting the presence of HBV as required by claims 21 and 25.

Response to Arguments

In the reply dated August 18, 2010, applicant argues that the Zaaijer et al. does not describe a kit comprising a means for detecting an HBV polynucleic acid comprising a serine at position 204. All of applicant's arguments have been fully considered but not found persuasive.

Zaaijer et al. teaches extracting DNA from serum or plasma using phenol-chloroform extraction and ethanol precipitation. Zaaijer et al. also teaches a means for detecting HBV reverse transcriptase nucleic acid (e.g., PCR and hybridization). It is noted that the claims do not require detection of the serine at position 204 (or methionine at 180 and serine at 204), but instead the claims require detecting HBV

nucleic acid that is suspected of having a serine a position 204 (or methionine at 180 and serine at 204). The methods of Zaaijer et al. are sufficient to detect HBV reverse transcriptase nucleic acid carrying a mutation at 204 or carrying a mutation at any other position.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allen et al. (Hepatology, 1998;27:1670-1677).

The claims are directed to a diagnostic kit for detecting the presence of an HBV in a biological sample, said kit comprising a means for detecting the presence of an

HBV polynucleic acid comprising a reverse transcriptase encoding domain, said reverse transcriptase encoding domain comprising a serine encoding codon at position 204; the diagnostic kit comprising:

(i) a means for obtaining the nucleic acid sequence of a target HBV polynucleic acid suspected to comprise a serine-encoding codon at position 204 of the HBV reverse transcriptase domain or to comprise a methionine-encoding codon at position 180 and a serine-encoding codon at position 204 of the HBV reverse transcriptase domain; and

(ii) a means for inferring, from the nucleic acid sequence obtained in (i), the presence of said serine-encoding codon at position 204 of the HBV reverse transcriptase domain or of said methionine-encoding codon at position 180 and said serine-encoding codon at position 204 of the HBV reverse transcriptase domain and, therefrom, the presence in said biological sample of said HBV.

It is noted that the claims are interpreted as being directed to a kit for detecting the presence of HBV reverse transcriptase polynucleic acid, the kit comprising a means for obtaining the nucleic acid sequence of the HBV polynucleotide.

Allen et al. teaches obtaining and sequencing HBV DNA using primers that fall within the HBV polymerase gene. Thus, Allen et al. teaches detecting the presence of HBV reverse transcriptase polynucleic acid in a sample using a means (e.g., sequencing primers) for obtaining the nucleic acid sequence of the HBV polynucleotide.

Allen et al. does not specifically teach a kit. However, the concept of packaging components into a kit is well known and routine in the art. It would have been obvious to one of ordinary skill in the art at the time the invention was made to package

components into a kit. One would be motivated to do this for commercial exploitation of the invention by providing convenience for the end user. Thus, the claimed invention is obvious over Allen et al.

The inferring step does not recite any additional active method steps, but simply states a characterization or conclusion of the previous step(s) or may be performed entirely in the human mind. One observing the claimed method being performed would not know if or when the inferring step has occurred. There is no active method step to observe after step (ii) (obtaining the nucleic acid sequence). Therefore, the "inferring" step or clause is not found to further limit the method defined by the claims, since it simply expresses the intended result of a positively recited process step.

It is suggested that applicant amends part (ii) of claims 22 and 26 to recite "analyzing the nucleic acid sequence obtained in (ii) for the presence of . . . ."

Claims 3 and 7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on (571) 272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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